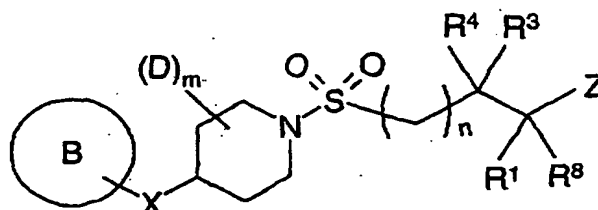


**CLAIMS:**

What we claim is:-

1. A compound of formula (1):



formula (1)

wherein:

Z is selected from  $-\text{CONR}^{15}\text{OH}$  and  $-\text{N}(\text{OH})\text{CHO}$ ;

$\text{R}^{15}$  is hydrogen or  $\text{C}_{1-3}$ alkyl;

$\text{R}^1$  is hydrogen or a group selected from  $\text{C}_{1-6}$ alkyl,  $\text{C}_{2-6}$ alkenyl,  $\text{C}_{2-6}$ alkynyl,  $\text{C}_{3-7}$ cycloalkyl,  $\text{C}_{5-7}$ cycloalkenyl, aryl and heteroaryl where the group is optionally substituted by one or more substituents independently selected from halo, nitro, cyano, trifluoromethyl, trifluoromethoxy,  $\text{C}_{1-4}$ alkyl,  $\text{C}_{2-4}$ alkenyl,  $\text{C}_{2-4}$ alkynyl,  $\text{C}_{3-6}$ cycloalkyl (optionally substituted by one or more  $\text{R}^{17}$ ), aryl (optionally substituted by one or more  $\text{R}^{17}$ ), heteroaryl (optionally substituted by one or more  $\text{R}^{17}$ ), heterocyclyl,  $\text{C}_{1-4}$ alkoxycarbonyl,  $-\text{OR}^5$ ,  $-\text{SR}^2$ ,  $-\text{SOR}^2$ ,  $-\text{SO}_2\text{R}^2$ ,  $-\text{COR}^2$ ,  $-\text{CO}_2\text{R}^5$ ,  $-\text{CONR}^5\text{R}^6$ ,  $-\text{NR}^{16}\text{COR}^5$ ,  $-\text{SO}_2\text{NR}^5\text{R}^6$  and  $-\text{NR}^{16}\text{SO}_2\text{R}^2$ ;

$\text{R}^{16}$  is hydrogen or  $\text{C}_{1-3}$ alkyl;

$\text{R}^{17}$  is selected from halo,  $\text{C}_{1-6}$ alkyl,  $\text{C}_{3-6}$ cycloalkyl and  $\text{C}_{1-6}$ alkoxy;

$\text{R}^2$  is group selected from  $\text{C}_{1-6}$ alkyl,  $\text{C}_{3-6}$ cycloalkyl,  $\text{C}_{5-7}$ cycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryl $\text{C}_{1-4}$ alkyl and heteroaryl $\text{C}_{1-4}$ alkyl where the group is optionally substituted by one or more halo;

$\text{R}^5$  is hydrogen or a group selected from  $\text{C}_{1-6}$ alkyl,  $\text{C}_{3-6}$ cycloalkyl,  $\text{C}_{5-7}$ cycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryl $\text{C}_{1-4}$ alkyl and heteroaryl $\text{C}_{1-4}$ alkyl where the group is optionally substituted by one or more halo;

$\text{R}^6$  is hydrogen,  $\text{C}_{1-6}$ alkyl or  $\text{C}_{3-6}$ cycloalkyl;

or  $\text{R}^5$  and  $\text{R}^6$  together with the nitrogen to which they are attached form a heterocyclic 4- to 7-membered ring;

$\text{R}^8$  is hydrogen or a group selected from  $\text{C}_{1-6}$ alkyl,  $\text{C}_{3-7}$ cycloalkyl and  $\text{C}_{5-7}$ cycloalkenyl where the group is optionally substituted by one or more substituents independently selected from halo, nitro, cyano, trifluoromethyl, trifluoromethoxy and  $\text{C}_{1-4}$ alkyl;

-71-

~~R<sup>3</sup> and R<sup>4</sup> are both hydrogen;~~

n is 0 or 1;

m is 0 or 1;

D is hydrogen, C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl or fluoro;

5 X is O, S, SO or SO<sub>2</sub>;

B is monocyclic aryl or heteroaryl where each is substituted in an ortho position by, and is optionally further substituted by one or more groups independently selected from nitro, trifluoromethyl, trifluoromethoxy, halo, C<sub>1-4</sub>alkyl (optionally substituted by R<sup>13</sup>), C<sub>2-4</sub>alkenyl (optionally substituted by R<sup>13</sup>), C<sub>2-4</sub>alkynyl (optionally substituted by R<sup>13</sup>), C<sub>3-6</sub>cycloalkyl (optionally substituted by R<sup>13</sup>), C<sub>3-6</sub>cycloalkenyl (optionally substituted by R<sup>13</sup>), phenyl (optionally substituted by halo or C<sub>1-4</sub>alkyl), heteroaryl (optionally substituted by halo or C<sub>1-4</sub>alkyl), heterocyclyl (optionally substituted by halo or C<sub>1-4</sub>alkyl), C<sub>1-4</sub>alkylthio, C<sub>3-6</sub>cycloalkylthio, -SOR<sup>13</sup>, -SO<sub>2</sub>R<sup>13</sup>, -SO<sub>2</sub>NHR<sup>13</sup>, -SO<sub>2</sub>NR<sup>13</sup>R<sup>14</sup>, -NHSO<sub>2</sub>R<sup>13</sup>, -NR<sup>13</sup>SO<sub>2</sub>R<sup>14</sup>, -NHCONHR<sup>13</sup>, -NHCONHR<sup>13</sup>R<sup>14</sup>, -OR<sup>13</sup>, cyano, -CONR<sup>13</sup>R<sup>14</sup>, -NHCOR<sup>13</sup>, -CO<sup>2</sup>R<sup>13</sup> and -

15 CH<sub>2</sub>CO<sub>2</sub>R<sup>13</sup>;

or B is bicyclic aryl or heteroaryl where each is optionally substituted by one or more groups independently selected from nitro, trifluoromethyl, trifluoromethoxy, halo, C<sub>1-4</sub>alkyl (optionally substituted by R<sup>13</sup>), C<sub>2-4</sub>alkenyl (optionally substituted by R<sup>13</sup>), C<sub>2-4</sub>alkynyl (optionally substituted by R<sup>13</sup>), C<sub>3-6</sub>cycloalkyl (optionally substituted by R<sup>13</sup>), C<sub>3-6</sub>cycloalkenyl (optionally substituted by R<sup>13</sup>), C<sub>1-4</sub>alkylthio, C<sub>3-6</sub>cycloalkylthio, -SOR<sup>13</sup>, -SO<sub>2</sub>R<sup>13</sup>, -SO<sub>2</sub>NHR<sup>13</sup>, -SO<sub>2</sub>NR<sup>13</sup>R<sup>14</sup>, -NHSO<sub>2</sub>R<sup>13</sup>, -NR<sup>13</sup>SO<sub>2</sub>R<sup>14</sup>, -NHCONHR<sup>13</sup>, -NHCONHR<sup>13</sup>R<sup>14</sup>, -OR<sup>13</sup>, cyano, -CONR<sup>13</sup>R<sup>14</sup> and -NHCOR<sup>13</sup>;

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R<sup>13</sup> and R<sup>14</sup> are independently hydrogen, C<sub>1-6</sub>alkyl or C<sub>3-6</sub>cycloalkyl;

or R<sup>13</sup> and R<sup>14</sup> together with the nitrogen to which they are attached form a heterocyclic 4 to

25 7-membered ring.

or a pharmaceutically acceptable salt thereof.

2. A compound according to claim 1 wherein B is phenyl or pyridyl where each is substituted in an ortho position by, and is optionally further substituted by one or more groups independently selected from halo, trifluoromethyl, cyano, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkyl, nitro, aryl, heteroaryl, heterocyclyl, *N*-(C<sub>1-4</sub>alkyl)carbamoyl and *N,N*-(C<sub>1-4</sub>alkyl)<sub>2</sub>carbamoyl; or B is naphthyl, quinolinyl, thieno[2,3-*d*]pyrimidinyl or thieno[3,2-*d*]pyrimidinyl each being

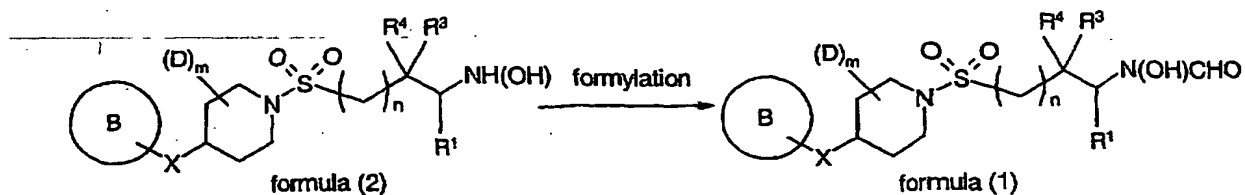
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-72-

optionally substituted by one or more groups independently selected from halo, trifluoromethyl, cyano, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkyl, aryl, heteroaryl, heterocyclyl and nitro.

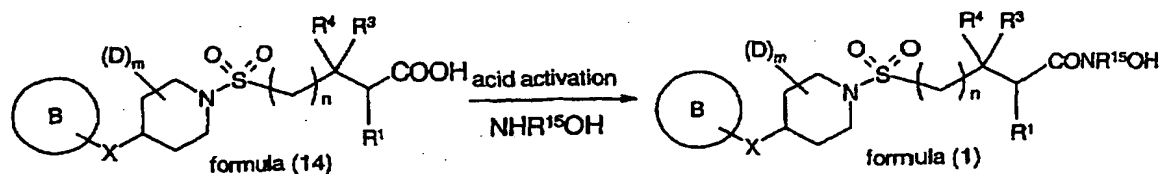
3. A compound according to claim 1 or 2 wherein R<sup>1</sup> is a group selected from C<sub>1-6</sub>alkyl,  
5 C<sub>3-6</sub>cycloalkyl, aryl, heteroaryl and C<sub>1-6</sub>alkyl substituted by aryl or heteroaryl wherein any R<sup>1</sup>  
group is optionally substituted by one or more substituents independently selected from halo,  
C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkyl and C<sub>3-6</sub>cycloalkyl.
4. A compound according to any one of claims 1 to 3 wherein X is O.
- 10 5. A compound according to any one of claims 1 to 4 for use as a medicament.
6. The use of a compound according to any one of claims 1 to 4 in the manufacture of a  
medicament in the treatment of a disease condition mediated by one or more  
15 metalloproteinase enzymes.
7. The use of a compound according to any one of claims 1 to 4 in the manufacture of a  
medicament in the treatment of a disease condition mediated TNF $\alpha$ .
- 20 8. A pharmaceutical composition comprising a compound according to any one of claims  
1 to 4; and a pharmaceutically-acceptable diluent or carrier.
9. A method of treating autoimmune disease, allergic/atopic diseases, transplant  
rejection, graft versus host disease, cardiovascular disease, reperfusion injury and malignancy  
25 in a warm-blooded animal, such as man, in need of such treatment which comprises  
administering to said animal an effective amount of a compound according to claim 1.
10. A process for preparing a compound of formula (1) according to claim 1 comprising,  
when Z is -N(OH)CHO, the step of:  
30 a) converting a hydroxylamine of formula (2) into a compound of formula (1);

-73-



or when Z is -CONR<sup>15</sup>OH, the step of:

b) converting an acid of formula (14) into a compound of formula (1);



5 and thereafter if necessary:

- i) converting a compound of formula (1) into another compound of formula (1);
- ii) removing any protecting groups;
- iii) forming a pharmaceutically acceptable salt or *in vivo* hydrolysable ester.